UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/691,895 | 10/23/2003 | Hans-Joerg Mocbius | MERZ 36 | 9019 |

25666 7590 08/29/2007

THE FIRM OF HUESCHEN AND SAGE
SEVENTH FLOOR, KALAMAZOO BUILDING
107 WEST MICHIGAN AVENUE
KALAMAZOO, MI 49007

| EXAMINER | |
|---|---|
| OLSON, ERIC | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 08/29/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/691,895 | MOEBIUS, HANS-JOERG | |
| | Examiner | Art Unit | |
| | Eric S. Olson | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *57-59,67-70 and 72-74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *57-59,67-70 and 72-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *June 29, 2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**Detailed Action**

This office action is a response to applicant's communication submitted June 29, 2007, wherein claims 57, 67, 68, and 72 are amended and claims 37-56, 60-66, and 71 are cancelled. This application claims benefit of provisional application 60/420918, filed October 24, 2002.

Claims 57-59, 67-70, and 72-74 are pending in this application.

Claims 57-59, 67-70, and 72-74 as amended are examined on the merits herein.

Applicant's amendment, submitted June 29, 2007, with respect to the rejection of instant claim 56 under 35 USC 101 for reciting a use without setting forth any steps involved in the claimed method or process, has been fully considered and found to be persuasive to remove the rejection as the rejected claim has been cancelled. Therefore the rejection is withdrawn.

Applicant's amendment, submitted June 29, 2007 with respect to the rejection of claims 56-61, 66, and 70-74 under 35 USC 112, second paragraph, for reciting the indefinite limitation, "aminocyclohexane derivatives" has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to recite only certain specific derivatives having a well-defined structure. Therefore the rejection is withdrawn.

Applicant's amendment, submitted June 29, 2007 with respect to the rejection of claims 56-60 and 66-74 under 35 USC 112, first paragraph, for lacking enablement for all possible dementias associated with a CNS disorder, has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to remove any intended use from the compositions. Therefore the rejection is withdrawn.

Applicant's amendment, submitted June 29, 2007 with respect to the rejection of claims 56-61 and 66-74 under 35 USC 112, first paragraph, for lacking enablement for a combination of any acetylcholinesterase inhibitor with any aminocyclohexane derivative, has been fully considered and found to be persuasive to remove the rejection as the claims have been amended to recite specific, limiting acetylcholinesterase inhibitors and aminocyclohexane derivatives. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 57-59, 67-70, and 72-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gold et al. (US patent 6071966, cited in PTO-892) in view of Dooley et al. (Reference included with PTO-892) Gold et al. discloses a pharmaceutical

composition comprising a compound having a structure identical to the aminocyclohexane derivatives of instant claims 66 and 67. (column 4, line 22 – column 6, line 5) For example, the compounds 1-amino-1,3,5-trimethylcyclohexane (neramexane), 1-amino-1,3,3,5-tetramethylcyclohexane, and 1-amino-1,3,3,5,5-pentamethylcyclohexane, are compounds of the claimed invention that are explicitly taught by Gold et al. Examples of pharmaceutical compositions of Gold et al. include tablets with 10 mg of active agent (column 21, lines 20-35) and an injectable solution with 12 mg of active agent. (column 22, lines 15-25) The compositions are disclosed to be useful for the treatment of neurodegenerative diseases including Alzheimer's disease. (column 36, lines 31-52) Gold et al. does not disclose a composition of this type further comprising an acetylcholinesterase inhibitor.

Dooley et al. discloses that Donepezil is a reversible acetylcholinesterase inhibitor that is indicated in the management of patients with mild to moderate Alzheimer's disease. (p. 206, left column, second paragraph) Gold et al. also discloses hat a dose of 5 or 10 mg of donepezil per day significantly improved cognition in patients with mild to moderate Alzheimer's disease. (p. 213, right column, second paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to add 5 or 10 mg of donepezil to the pharmaceutical compositions of Gold et al. One of ordinary skill in the art would have been motivated to modify the invention in this manner because the prior art discloses that donepezil and the compounds of Gold et al. are both useful for the same purpose, namely treating Alzheimer's disease. One

of ordinary skill in the art would reasonably have expected success because both compounds are known in the prior art to be effective individually for this purpose. It has been held that it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third composition for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Thus the invention taken as a whole is *prima facie* obvious.

Response to Argument: Applicant's argument, submitted June 29, 2007, with respect to the above ground of rejection, has been fully considered and not found to be persuasive to remove the rejection. Applicant argues that the claimed compositions produce the unexpected result of being effective to produce clinical improvement in Alzheimer's patients. First, it is noted that the results Applicant points to in the specification (example 1, pp. 69-73) use memantine, an aminoadamantane that is not included within the limitations of the elected invention. According to MPEP 716.02(d), Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." In other words, the showing of unexpected results must be reviewed to see if the results occur over the entire claimed range. In re Clemens, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980) See also In re Peterson, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003); In re Grasselli, 713 F.2d 731, 741, 218USPQ 769, 777

(Fed. Cir. 1983) Because no compounds falling within the scope of the elected invention were tested these results are not seen to be persuasive to demonstrate unexpected results.

Furthermore, the results seen in example 1 and in the reference Tairot et al. included with form PTO-1449, do not serve do demonstrate an unexpected result greater than what would be expected from the additive combination of the two components. Example 1 in the specification is a survey of clinical results for combination therapy. The scale used was an unidentified four-point scale measuring the general clinical impression of the physician after a period of about half a year, or around 26 weeks. No control group is included for acetylcholinesterase inhibitors alone, and the magnitude or duration of improvement is not shown. For Tairot et al. patients are measured for 24 weeks by several measures including the SIB, ADCS-ADL, and CIBC-plus to compare memantine plus donepezil to memantine plus placebo. (p. 322, figures 2 and 3) Although the SIB score improved temporarily, the combination therapy only led to a reduced rate of decline in the ADCS-ADL and CIBC-plus scores. Also, the SIB score was seen to resume its decline after about 12 weeks, indicating that the reversal of decline was not permanent. Although Applicant claims that the data demonstrate an improvement in function that could not be achieved with monotherapy of either drug alone, the prior art shows that it is indeed possible to produce a temporary improvement in function using donepezil alone. For example, Feldman et al. (Reference included with PTO-892) discloses a study of donepezil monotherapy that led to a clinical improvement in the SIB and sMMSE scores after 24 weeks. (p. 617, left

column ,figure 3) Gauthier et al. (Reference included with PTO-892) also discloses similar results for donepezil monotherapy. (p. 350, figure 2) In view of these results, the clinical improvement demonstrated in the instant specification is not shown to be anything beyond the additive effects expected based on the prior art. Therefore no unexpected results are seen and the rejection is maintained and made **FINAL**.

## Conclusion

No claims are allowed in this application. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson
Patent Examiner
AU 1623
8/21/07

Anna Jiang
8/24/07
Supervisory Patent Examiner
AU 1623